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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,978	04/24/2007	Geoffrey Gerard Hayes	Y2440-00004	4150

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EXAMINER	
BROWE, DAVID	
ART UNIT	PAPER NUMBER
4131	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,978	HAYES ET AL.	
	Examiner	Art Unit	
	DAVID M. BROWE	4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *138-164* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *138-164* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *August 10, 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *October 31, 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 138-164 are pending and under examination.

Foreign Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Certified copies has been filed in parent Application Nos. 0403100.1 and 0501638.1, filed on February 12, 2004 and January 28, 2005, respectively.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 138-164 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oshlack *et al.* (U.S. Patent No. 5,958,452) in view of Oshlack *et al.* (U.S. Patent Application Pub. No. 20020010127).

Applicant Claims

Applicants claim a controlled-release unit dose rubbery matrix comprising a neutral poly(ethyl acrylate, methyl methacrylate) copolymer and an active agent. The active agent can be an opioid, a stimulant, a barbiturate, an anti-depressant, a dissociative anesthetic, or combinations thereof. The opioid, such as oxycodone in an amount from 5-160 mg, can be in combination with an opioid antagonist, such as naltrexone. The controlled-release matrix can include at least one other release-modifying polymer, such as an alkyl cellulose, particularly ethyl cellulose, or a water insoluble ammonium methacrylate copolymer. The matrix can further include a plasticizer, a lubricant, a bulking agent, and an agent which imparts resistance to active agent extraction by common solvents. The controlled-release unit dose can be obtained by melt-extrusion, and formulated as multi-particulate dosage forms suited for once or twice a day dosing. Controlled-release unit doses containing oxycodone can be specifically formulated to exhibit desired *in vitro* oxycodone dissolution rates; as assessed by standard USP Paddle or Basket Methods at 100 rpm, 900 ml aqueous

buffer, pH 1.2 or 1.6-7.2, and 37ºC; and to deliver the peak plasma level of oxycodone *in vivo* at 2-17 hours after administration of the dosage form.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Oshlack *et al.* (U.S. Patent No. 5,958,452) disclose a controlled-release unit dose matrix comprising a pharmaceutically acceptable acrylic-methacrylic acid copolymer and an active agent (Col. 3, lns. 43-44, 61-65; Col. 4, lns. 5-6, 10-11, 17-20, 31-33; Col. 6, lns. 50-53; Col. 8, lns. 36-39, 43-44, 47-49, 53-56). The acrylic-methacrylic acid copolymers disclosed for use in a preferred embodiment inherently encompasses a neutral poly(ethyl acrylate, methyl methacrylate) copolymer (Col. 8, lns. 36-62). The active agent can be any water-soluble or water-insoluble drug, and include opioid analgesics, stimulants, hypnotics (which includes barbiturates and dissociative anesthetics), psychotropics (which includes anti-depressants), and sedatives (Col. 6, lns. 50-53, 56-57; Col. 7, lns. 5-8, 9-11, 25). In preferred embodiments, the opioid analgesic is oxycodone in an amount from about 5-400 mg (Col. 7, lns. 35-37, 54-56). The controlled-release matrix can include at least one other release-modifying polymer, such as an alkyl cellulose, particularly ethyl cellulose, or a water-insoluble ammonium methacrylate copolymer (Col. 8, lns. 36-59).

In addition to the acrylic-methacrylic acid copolymer and active agent, the matrix can include suitable quantities, up to about 50 wt%, of other materials such as plasticizers, lubricants, diluents, binders, and granulating aids, such as bulking agents (Col. 9, lns. 40-52). The most suitable plasticizer is based on its ability to lower the glass transition temperature (Tg) of the polymer (Col. 6, lns. 30-34), which would impart a

rubbery consistency to the controlled-release unit dose matrix in ambient conditions. The matrix may also include retardant materials, such as water-insoluble wax-like thermoplastic substances possibly mixed with one or more wax-like thermoplastic substances that are sparingly water-permeable (Col. 8, lns. 66-67; Col. 9, lns. 1-3), which are known in the art to confer a resistance to *in vitro* extraction of the active agent with common solvents, such as alcohol (Col. 4, lns. 11-16).

The controlled-release unit dose can be obtained by melt-extrusion, and formulated as multi-particulate dosage forms suited for once (every 12 hours) or twice (every 24 hours) a day dosing (Col. 3, lns. 50-53, 61-67; Col. 4, lns. 1-3, 5-6, 10, 39-41, 50-53; Col. 11, lns. 61-63). Controlled-release unit doses containing oxycodone can be specifically formulated to exhibit desired *in vitro* oxycodone dissolution rates; as assessed by standard USP Paddle or Basket Methods at 100 rpm, 900 ml aqueous buffer, pH 1.2 or 1.6-7.2, and 37°C (Col. 9, lns. 44-46; Col. 11, lns. 33-48, 61-67; Col. 12, lns. 1-7, 13-16, 22-27); and to deliver the peak plasma level of oxycodone *in vivo* at 2-17 hours after administration of the dosage form (Col. 12, lns. 9-10, 15-17).

Oshlack *et al.* (U.S. Patent Application Pub. No. 20020010127) disclose a controlled-release unit dose matrix comprising a methacrylic acid-ethyl acrylate copolymer and an opioid agonist, such as oxycodone, in combination with an opioid antagonist, such as naltrexone (Pg. 1, sec. 0009, 0011, 0016; Pg. 2, sec. 0018; Pg. 10, sec. 0107; Pg. 13, sec. 0135, 0137; Pg. 14, sec. 0148). The controlled-release matrix can include at least one other release-modifying polymer, such as an alkyl cellulose, particularly ethyl cellulose, or a water insoluble ammonium methacrylate copolymer (Pg.

13, secs. 0136-0137; Pg. 14, secs. 0144-0145, 0149). The matrix can further include a plasticizer, a lubricant, a granulating aid, such as a bulking agent, and an agent which imparts resistance to active agent extraction by common solvents (Pg. 13, sec. 0140; Pg. 14, secs. 0146, 0151-0152). The controlled-release unit dose can be obtained by melt-extrusion, and formulated as multi-particulate dosage forms suited for once or twice a day dosing (Pg. 2, sec. 0024; Pg. 14, sec. 0149, 0153; Pg. 15, sec. 0156). Controlled-release unit doses containing oxycodone can be specifically formulated to exhibit desired *in vitro* oxycodone dissolution rates; as assessed by standard USP Paddle or Basket Methods at 100 rpm, 900 ml aqueous buffer, pH 1.2 or 1.6-7.2, and 37ºC (Pg. 2, sec. 0023; Pg. 10, sec. 0105; Pg. 13, sec. 0135; Pg. 15, sec. 0162).

Ascertainment of the Difference Between the Scope of the Prior Art and the Claims (MPEP §2141.012)

Oshlack *et al.* (U.S. Patent No. 5,958,452) disclose a controlled-release unit dose matrix, that, in one embodiment, could be made to have a rubbery consistency and include a neutral poly(ethyl acrylate, methyl methacrylate) copolymer with an active agent. The matrix can include any active agent, release-modifying polymer, thermoplastic retardant or combination thereof, and excipient(s) specified in the present invention. Furthermore, like applicants' invention, the matrix can be obtained by melt-extrusion, and formulated as multi-particulate dosage forms suited for once or twice a day dosing. Controlled-release unit doses containing oxycodone can, through routine optimization procedures, be specifically formulated to exhibit the stipulated *in vitro* oxycodone dissolution rates, and to deliver peak plasma levels of oxycodone *in vivo* at

2-17 hours after administration of the dosage form. Oshlack *et al.* (U.S. Patent No. 5,958,452), however, lacks the explicit teaching of combining the opioid active agent with an opioid antagonist in the same controlled-release unit dose. This deficiency is cured by the teaching of Oshlack *et al.* (U.S. Patent Application Pub. No. 20020010127), that by combining an opioid agonist and an opioid antagonist together can impart improved analgesic effects as compared to an opioid agonist alone.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of the present invention to combine the teachings of Oshlack *et al.* (U.S. Patent No. 5,958,452) and Oshlack *et al.* (U.S. Patent Application Pub. No. 20020010127) to deduce the applicants' current invention. Since Oshlack *et al.* (U.S. Patent Application Pub. No. 20020010127) report that combining optimal amounts of an opioid agonist, such as oxycodone, and an opioid antagonist, such as naltrexone, in the same controlled-release oral dosage form can impart enhanced analgesic potency while attenuating unwanted side effects (Pg. 3, sec. 0025), the skilled artisan would be motivated to modify the teachings of Oshlack *et al.* (U.S. Patent No. 5,958,452) by incorporating an optimal amount of an opioid antagonist, with the reasonable expectation that such a modification would enhance analgesic potency and attenuate the unwanted side effects, such as nausea and vomiting, that typically occur in patients taking analgesic opioid medications. Applicants have no allegations of surprising or

unexpected results. Therefore, the claimed invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID M. BROWE whose telephone number is 571-270-1320. The examiner can normally be reached on Monday-Friday 7:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick J. Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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